

REMARKS/ARGUMENTS

Claims 1-14 are pending. Claims 1, 2, 4 and 8 have been withdrawn from consideration. Claims 3 and 5-7 are subject to examination. The Applicants submit that new Claims 9 and 10 also conform to the prior restriction and election requirement and should be examined. Examination of new Claims 11-14 is also requested, upon an indication of allowability for the elected species.

Independent Claim 3 has been revised to recite active steps and for clarity as discussed with the Examiners. New Claims 9-14 find support in original Claim 3 and in the specification, e.g., in Example 3. Accordingly, the Applicants do not believe that any new matter has been added.

The Applicants thank Examiners Switzer and Fredman for the helpful and courteous discussion of January 21, 2004. It was suggested that the claim language be revised for clarity, for example, to recite active steps, and that the Applicants point out why selection of particular oligonucleotides might provide some benefit that selection of other portions of the VT1 nucleic acid sequence would not. The Applicants have now revised the claim language as suggested and point out experimental data showing the superior results provided by the selection of particular oligonucleotides, such as the oligonucleotides comprising the elected SEQ ID NOS: 2 and 15. Favorable consideration is now respectfully requested.

Election/Restriction

The Applicants confirm their election with traverse of:

| | |
|------------------------------------|------------------------------|
| Restriction Group: | Group III, Claims 3 and 5-7; |
| Species of first oligonucleotide: | SEQ ID NO: 2; |
| Species of second oligonucleotide: | SEQ ID NO: 15. |

Claim 3 is generic.

The traverse is on the grounds that the products of Groups I and III are interrelated verotoxin (VT) sequences and may be examined together without undue burden and that the products and processes of Groups I and II, and products and methods of Groups III and IV, are interrelated and may be examined together without undue burden. New Claims 11-15 have been added. Claims 11 and 12 are directed to nonelected species of oligonucleotides. The Applicants respectfully request that examination be extended to these claims upon an indication of allowability for generic Claim 3. Claims 13-14 are composition claims. Since these claims are directed to specific combinations of oligonucleotides which provide superior results in the claimed processes as shown below, and may be searched without undue burden, the Applicants respectfully request that these claims be considered along with the elected process claims.

Claim Objections

Claims 3 and 5 were objected to for various informalities. These objections are moot in view of the amendment of these claims.

Rejection—35 U.S.C. § 112, second paragraph

Claims 3, 5, 6 and 7 were rejected under 35 U.S.C. 112, second paragraph as being indefinite. These rejections are moot in view of the amendments above.

Rejection—35 U.S.C. § 103

Claim 3 was rejected under 35 U.S.C. 103 as being unpatentable over Bekkaoui et al., U.S. Patent No. 6,136,533, in view of all of the following: Gilgen et al., Res. in Microbiol. 149:145; Calderwood et al., PNAS 84: 4364, and Buck et al., Biotechniques 27:528. The

cited prior art does not anticipate or render obvious the present invention for the following reasons.

Bekkaoui does not disclose or suggest a method for detecting VT1 RNA or disclose or suggest the oligonucleotides of SEQ ID NO: 2 or 15. The Official Action argues that Gilgen, Calderwood and Buck disclose amplification of the VT1 gene, disclose the full-length VT-1 gene sequence and expressly disclose the equivalence of different parts of a known nucleic acid sequence as primers. However, none of the cited prior art discloses or suggests selecting the particular oligonucleotides of the present invention.

Moreover, the Applicants disagree that the cited prior art would suggest or motivate one with ordinary skill in the art to apply the method of Bekkaoui to the detection of the VT1 gene, especially by using the specific oligonucleotides disclosed by the present specification. These oligonucleotides as shown, for example, in Figure 3, provide superior RNA amplification results compared to other oligonucleotides. Thus, based on this data the Applicants respectfully disagree that all oligonucleotides are equivalents.

Presently, the invention has been examined as directed to Group III and as it reads on SEQ ID NOS: 2 and 15. The surprising and superior RNA amplification results provided by this combination of oligonucleotides are shown in Fig. 3, lanes 1-3 (lane 4 is a control). Fig. 3 is reproduced on the following page.

Fig. 3, lanes 1-3, show the RNA amplification obtained by using primers comprising SEQ ID NOS: 2 and 15. Heavy and clear banding is quite evident in these lanes in comparison with banding produced by other oligonucleotide combinations, e.g., in lanes 5-7 or 9-11 (lanes 4, 8 and 12 are controls). See also, Fig. 4, lanes 1-3, 5-7 and 9-11 (lanes 4, 8 and 12 are controls).

As disclosed in the specification starting on page 12, line 16, Fig. 3 shows amplification reactions for VT1 RNA performed as described in Example 3. Lanes 1-4 use “combination (a)” which uses oligonucleotides comprising SEQ ID NOS: 2 and 15 “combination (a)” in Example 3¹. Compared to other oligonucleotide combinations such as (b), and (c) shown in Figs. 3 and 4, combination (a) provided cleaner and more distinct banding. Thus, selection of a process using oligonucleotides comprising SEQ ID NOS: 2 and 15 provides a superior NASBA result compared to other oligonucleotide combinations.

While the selection of the combination of oligonucleotides of SEQ ID NOS: 2 and 15 provided the best results among those combinations in Table 3, other combinations, also provide superior results compared to selection of oligonucleotides which are excluded from the scope of the invention. The Applicants also respectfully request consideration of the superior results provided by these other combinations. Accordingly, as there is no suggestion in the prior art to combine the teachings of the cited documents, nor any suggestion of the superior results provided by selecting particular oligonucleotide sequences, the Applicants respectfully request that this rejection be withdrawn for the elected invention and that examination be extended to additional species falling within generic Claim 3.

¹ In Combination (a), “6R is SEQ ID NO: 2; 5F comprises SEQ ID NO: 15 but includes an RNA polymerase promoter site and may also be identified as SEQ ID NO: 36; 5S, the so-called first oligonucleotide, SEQ ID NO: 27, is merely a probe designed on the basis of the binding site of the VT1 RNA to cut the VT1 RNA and does not directly affect the amplification results. Thus, Combination (a) involves oligonucleotides comprising the elected SEQ ID NOS: 2 and 15.

Rejection—35 U.S.C. § 103

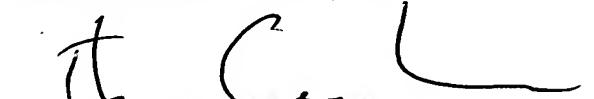
Claims 5-7 were rejected under 35 U.S.C. 103 as being unpatentable over Bekkaoui et al., U.S. Patent No. 6,136,533, in view of all of the following: Gilgen et al., Res. in Microbiol. 149:145; Calderwood et al., PNAS 84: 4364, and Buck et al., Biotechniques 27:528, as applied above, and further in view of Ishiguro et al., Nuc. Acid Res. 24:4992. The Applicants submit that this rejection may also be withdrawn in view of the arguments above. Ishiguro is cited for its disclosure of intercalator fluorescent dye and does not disclose or suggest selecting the oligonucleotides of the present invention for use in a method for detecting VT1 RNA.

CONCLUSION

In view of the above amendments and remarks the Applicants submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Norman F. Oblon
Attorney of Record
Registration No. 24,618

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/03)

Thomas M. Cunningham
Registration No. 45,394